

PATENT COOPERATION TREATY

PCT

INTERNATIONAL SEARCH REPORT

(PCT Article 18 and Rules 43 and 44)

Applicant's or agent's file reference VJR. VB60107	FOR FURTHER ACTION see Form PCT/ISA/220 as well as, where applicable, item 5 below.	
International application No. PCT/EP2004/001850	International filing date (day/month/year) 24/02/2004	(Earliest) Priority Date (day/month/year) 26/02/2003
Applicant GLAXOSMITHKLINE BIOLOGICALS S.A.		

This International Search Report has been prepared by this International Searching Authority and is transmitted to the applicant according to Article 18. A copy is being transmitted to the International Bureau.

This International Search Report consists of a total of 9 sheets.



It is also accompanied by a copy of each prior art document cited in this report.

1. Basis of the report

- a. With regard to the language, the international search was carried out on the basis of the international application in the language in which it was filed, unless otherwise indicated under this item.



The international search was carried out on the basis of a translation of the international application furnished to this Authority (Rule 23.1(b)).

- b. ☒ With regard to any nucleotide and/or amino acid sequence disclosed in the international application, see Box No. I.

2. ☒ Certain claims were found unsearchable (See Box II).

3. ☒ Unity of invention is lacking (see Box III).

4. With regard to the title,



the text is approved as submitted by the applicant.



the text has been established by this Authority to read as follows:

HYPOALLERGENIC DER P 1 AND DER P 3 PROTEINS FROM DERMATOGRAPHOIDES PTERONYSSINUS

5. With regard to the abstract,



the text is approved as submitted by the applicant.



the text has been established, according to Rule 38.2(b), by this Authority as it appears in Box No. IV. The applicant may, within one month from the date of mailing of this international search report, submit comments to this Authority.

6. With regard to the drawings,

- a. the figure of the drawings to be published with the abstract is Figure No. _____



as suggested by the applicant.



as selected by this Authority, because the applicant failed to suggest a figure.



as selected by this Authority, because this figure better characterizes the invention.

- b. ☒ none of the figures is to be published with the abstract.

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Box No. 1 Nucleotide and/or amino acid sequence(s) (Continuation of item 1.b of the first sheet)

1. With regard to any nucleotide and/or amino acid sequence disclosed in the international application and necessary to the claimed invention, the international search was carried out on the basis of:
 - a. type of material
 - ☒ a sequence listing
 - ☐ table(s) related to the sequence listing
 - b. format of material
 - ☒ in written format
 - ☒ in computer readable form
 - c. time of filing/furnishing
 - ☒ contained in the international application as filed
 - ☐ filed together with the international application in computer readable form
 - ☐ furnished subsequently to this Authority for the purpose of search
2. ☐ In addition, in the case that more than one version or copy of a sequence listing and/or table relating thereto has been filed or furnished, the required statements that the information in the subsequent or additional copies is identical to that in the application as filed or does not go beyond the application as filed, as appropriate, were furnished.
3. Additional comments:

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Box No. IV Text of the abstract (Continuation of item 5 of the first sheet)

The present invention provides a treatment for allergy comprising the provision of a recombinant Der p 1/ProDer p 1/PreProDer p 1 allergen derivative, ProDer p 3 or a recombinant ProDer p 3/Der p 3/ PreProDer p 3 allergen derivative with hypoallergenic activity. Pharmaceutical compositions comprising said mutant allergens which stimulate a Th1-type immune response in allergic or naïve individuals thereby reducing the potential for an allergic response upon contact with the wild-type allergen, are also provided.

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Box II Observations where certain claims were found unsearchable (Continuation of item 2 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☒ Claims Nos.: 30
because they relate to subject matter not required to be searched by this Authority, namely:
Although claim 30 directed to a method of treatment of the human/animal body, the search has been carried out and based on the alleged effects of the compound/composition.
2. ☒ Claims Nos.: 3, 19
because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:
see FURTHER INFORMATION sheet PCT/ISA/210
3. ☐ Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box III Observations where unity of invention is lacking (Continuation of item 3 of first sheet)

This International Searching Authority found multiple inventions in this International application, as follows:

see additional sheet

1. ☐ As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.
2. ☐ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3. ☐ As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:
4. ☒ No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:
1, 3-14, 20-28 and 30 partially

Remark on Protest

- ☐ The additional search fees were accompanied by the applicant's protest.
☐ No protest accompanied the payment of additional search fees.

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

This International Searching Authority found multiple (groups of) inventions in this international application, as follows:

1. claims: 1, 3-14, 20-28 and 30 partially

Hypoallergenic mutants of the Der p 1 protein of Dermatographoides pteronyssinus wherein cysteines have been mutated, nucleic acids encoding the same, vectors, methods and uses related thereto.

1.1. claims: 1, 3-14, 20-28 and 30 all partially

wherein the cysteine residue at position 71 has been mutated

1.2. claims: 1, 3-14, 20-28 and 30 partially

wherein the cysteine residue at position 103 has been mutated

1.3. claims: 1, 3-14, 20-28 and 30 partially

wherein the cysteine residue at position 117 has been mutated

2. claims: 2-14, 20-28, 30 partially

Hypoallergenic mutants of the Der p 1 protein of Dermatographoides pteronyssinus wherein amino acids 147-160 have been deleted (positions 227-240 of proDer p 1), nucleic acids encoding the same, vectors, methods and uses related thereto.

3. claims: 15-19, 29 completely; claims 20-28, 30 partially

Hypoallergenic mutants of the Der p 3 protein of Dermatographoides pteronyssinus wherein the protein has been either thermally treated or mutated (in particular at the positions corresponding to cystein residues), nucleic acids encoding the same, vectors, methods and uses related thereto.

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

Continuation of Box II.1

Although claim 30 directed to a method of treatment of the human/animal body, the search has been carried out and based on the alleged effects of the compound/composition.

Continuation of Box II.1

Claims Nos.: 30

Rule 39.1(iv) PCT - Method for treatment of the human or animal body by therapy

Continuation of Box II.2

Claims Nos.: 3,19

Claims 3 and 19 are directed to allergens having the sequences as set out in SEQ ID No. 15, 17 and 19. However, SEQ ID No. 15, 17 and 19 disclose oligonucleotides which cannot be regarded as allergens. It results that the claims are so unclear and their subject-matter is so unsufficiently disclosed that no search has been carried out for claims 3 and 19.

The applicant's attention is drawn to the fact that claims relating to inventions in respect of which no international search report has been established need not be the subject of an international preliminary examination (Rule 66.1(e) PCT). The applicant is advised that the EPO policy when acting as an International Preliminary Examining Authority is normally not to carry out a preliminary examination on matter which has not been searched. This is the case irrespective of whether or not the claims are amended following receipt of the search report or during any Chapter II procedure. If the application proceeds into the regional phase before the EPO, the applicant is reminded that a search may be carried out during examination before the EPO (see EPO Guideline C-VI, 8.5), should the problems which led to the Article 17(2) declaration be overcome.

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A. CLASSIFICATION OF SUBJECT MATTER

 IPC 7 C07K14/435 A61K38/43 C12N15/63 C12N9/64 C12N15/12
 C12N5/10

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC 7 C07K C12N

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

EPO-Internal, BIOSIS, EMBASE, WPI Data

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	WO 01/96385 A (SMITHKLINE BEECHAM BIOLOG ;BOLLEN ALEX (BE); JACOBS PAUL (BE); JAC) 20 December 2001 (2001-12-20) the whole document	1,3-14, 20-28,30
Y	WO 02/074250 A (PANACEA PHARMACEUTICALS ;RABJOHN PATRICK A (US); BANNON GARY A (US) 26 September 2002 (2002-09-26) the claims and Appendix 4	1,3-14, 20-28,30
Y	WO 99/25823 A (SMITHKLINE BEECHAM BIOLOG ;BOLLEN ALEX (BE); JACOBS PAUL (BE); BRU) 27 May 1999 (1999-05-27) page 6, line 30 - page 9; claim 10 ----- -/--	1,3-14, 20-28,30

☒ Further documents are listed in the continuation of box C.☒ Patent family members are listed in annex.

* Special categories of cited documents:

- *A* document defining the general state of the art which is not considered to be of particular relevance
- *E* earlier document but published on or after the International filing date
- *L* document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
- *O* document referring to an oral disclosure, use, exhibition or other means
- *P* document published prior to the international filing date but later than the priority date claimed

- *T* later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
- *X* document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
- *Y* document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.
- *G* document member of the same patent family

Date of the actual completion of the international search

2 July 2004

Date of mailing of the international search report

06. 06. 2005

Name and mailing address of the ISA

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C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT		
Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	JACQUET ALAIN ET AL: "Conversion of ProDer p 1 into a mature Der p 1 is an autocatalytic processing which is dependent of the cysteine proteinase activity of the allergen" JOURNAL OF ALLERGY AND CLINICAL IMMUNOLOGY, vol. 107, no. 2, February 2001 (2001-02), page S16, XP009032859 57th Annual Meeting of the American Academy of Allergy, Asthma and Immunology; New Orleans, Louisiana, USA; March 16-21, 2001 ISSN: 0091-6749 abstract	1,3-14, 20-28,30
Y	SHAKIB F ET AL: "The proteolytic activity of Der p 1 selectively enhances IgE synthesis: A link between allergenicity and cysteine protease activity" CLINICAL AND EXPERIMENTAL ALLERGY 2000 UNITED KINGDOM, vol. 30, no. 6, 2000, pages 751-752, XP002286891 ISSN: 0954-7894 the whole document	1,3-14, 20-28,30
P,X	WO 03/016340 A (GLAXOSMITHKLINE BIOLOG SA ; BOLLEN ALEX (BE); JACQUET ALAIN (BE); M) 27 February 2003 (2003-02-27) the whole document	1,3-14, 20-28,30
A	WO 92/04445 A (WESTERN AUSTRALIAN RES INST) 19 March 1992 (1992-03-19)	
A	JACQUET A ET AL: "Absence of immunoglobulin E synthesis and airway eosinophilia by vaccination with plasmid DNA encoding ProDer p 1." CLINICAL AND EXPERIMENTAL ALLERGY, vol. 33, no. 2, February 2003 (2003-02), pages 218-225, XP002286892 ISSN: 0954-7894 (ISSN print)	

INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No

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Patent document cited in search report		Publication date	Patent family member(s)	Publication date
WO 0196385	A	20-12-2001	AU 8384701 A	24-12-2001
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			CA 2091449 A1	12-03-1992
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			ES 2133288 T3	16-09-1999
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			JP 6500993 T	27-01-1994
			KR 274321 B1	15-12-2000
			US 6689876 B1	10-02-2004
			US 6423837 B1	23-07-2002
			US 6060057 A	09-05-2000
			US 5773002 A	30-06-1998
			US 5770202 A	23-06-1998
			US 5552142 A	03-09-1996
			US 6086897 A	11-07-2000
			US 6147201 A	14-11-2000
			US 5433948 A	18-07-1995